New Data Science in Nucleic Acids Chemistry (5): Effect of local environments on the stability of nucleic acids in mitochondria

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Molecular crowding affects the stability and conformation of nucleic acids (DNA and RNA),[1] leading to the formation of non-canonical DNA structures such as a guanine-quadruplex (G4) and i-motif that alter DNA replication and transcription and can cause diseases like cancer.[2] Although a link between molecular crowding and cellular function has been suggested, detailed information in localized region of the cells on this phenomenon is still lacking. For example, mitochondria, which are a key organelle for supplying the energy for the cell to exert all its functions, have own DNAs (mtDNAs). It has been suggested that G4s on mtDNAs have roles in regulation of replication and transcription of mtDNAs, which are vital for mitochondria functions. To clarify the roles of non-canonical structure in mitochondria, it is beneficial to predict the behavior of DNA structures depending on mitochondrial environment.

We have recently developed the stability prediction of DNA duplexes from their sequences in solutions containing different concentrations of cations and cosolutes.[3] As it has been suggested that the molecular crowding condition in mitochondria is more crowded with macromolecules than cytosol and nucleus,[4] we tested how the duplex formations could be predicted in the presence of polyethylene glycol (PEG) having large molecular weight like PEG8000. We found that the duplex formation having GC-rich sequence more destabilized in PEG8000 containing solution, compared with our prediction for in nucleus using PEG200 as a cosolute. Thus, the molecular environment in mitochondria may destabilize duplex and induce G4 formations more than that in nucleus. We are further investigating the effect on mitochondrial environment on G4 stability by using mitochondria-specific reporter assay and will discuss in the presentation.

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